REMARKS

Claims 1-10 are all the claims pending in the application; claims 1, 2 and 10 are rejected; claims 3-9 have been withdrawn from consideration.

Claims 3-9 have now been cancelled.

Claims 1, 2 and 10 have been amended to more fully place the claims in U.S. format and to cancel non-elected subject matter. Support for the amendment of claim 1 to recite homologues with at least 90% homology may be found in the specification at page 5, lines 8-14. Support for recitation of the activity of the polypeptides and fragments may be found in the specification at page 15, lines 18-20.

No new matter has been added. Entry of this amendment is respectfully requested.

I. Formal Matters

A. At paragraph 2 of the Office Action, the Examiner states that as no utility for the claimed protein is disclosed in any of the priority applications, the priority granted to the instant application is only the filing date of the instant application, i.e., December 4, 2001.

As discussed below, Applicants have established a specific, substantial and credible utility for the instant invention (as an anti-inflammatory) that is supported by the parent application, international application and Japanese priority application. Therefore, Applicants respectfully request the Examiner to grant priority to each of the prior applications, back to the Japanese priority application filed on October 7, 1997. Please see Applicants' further comments below under section **III.** for more discussion on this point.

B. Applicants thank the Examiner for returning an initialed and signed copy of the document list included with the Information Disclosure Statement (IDS) filed in this application

on December 18, 2002. Applicants note, however, the Examiner has not returned an acknowledged copy of the document list included with the IDS filed December 4, 2001. Therefore, Applicants respectfully request that an appropriately acknowledged copy of the document list filed December 4, 2001, be returned to Applicants.

II. Claim Objections

At paragraph 3 of the Office Action, the Examiner objects to claim 10 as depending, in part, from a non-elected claim. The Examiner also objects to claims 1 and 2 as containing a typographical error in the term "comprising" which should read "comprises."

In response, Applicants include herewith amendments to claims 1, 2 and 10 that fully address the points raised by the Examiner. In view of these amendments, Applicants respectfully request reconsideration and withdrawal of these objections.

III. Rejections of Claims Under 35 U.S.C. §101

At paragraph 5 of the Office Action, claims 1, 2 and 10 are rejected under 35 U.S.C. §101 as lacking a credible, substantial, specific, or well-established utility.

In response, Applicants note that the OHP106 polypeptide of the present invention set forth in SEQ ID NO:7 shares 100% homology with the MD-2 protein described in Shimazu et al. (1999), cited by the Examiner in the outstanding Office Action (paragraph 14) and listed on the Form PTO 892 included with the Office Action. A homology analysis is included with the instant Amendment.

The specification of the instant application states on page 15, lines 18-20 (with the same discussion found at page 14 of the Japanese priority document JP-A-9-274673) that the protein of the present invention may "suppress chronic or acute inflammation, such as, for example, that

associated with infection such as septic shock or systemic inflammatory response syndrome (SIRS)." Thus, the specification includes a clear utility for the protein of the present application (as an anti-inflammatory).

This utility is fully supported by a number of journal articles that were published well after the priority date of the present application. Included herewith are four publications which demonstrate the physiology of the protein of the present invention.

Briefly, Applicants note that Gram-negative bacteria have the ability to initiate septic shock in humans. LPS (lipopolysaccharide), which is the main component of the outer membrane of Gram-negative bacteria, is the initiator. The Toll-like receptor 4 (TLR4) complex expressed on the surface of cells such as monocytes is the receptor that recognizes LPS. Upon binding of the LPS, a cascade is initiated, leading to the development of septic shock.

The journal article included herewith establish that MD-2 is one of the proteins that associates with TLR4 to form the TLR4 complex. MD-2 is secreted by cells to the extracellular space where it acts as a soluble receptor which binds to an extracellular part of TLR4 (Visintin et al., 2001). MD-2 can then specifically recognize LPS (Akashi et al., 2001) and binds to LPS with high affinity (Viriyakosol et al., 2001). As a result, the cellular response to LPS, mediated by TLR4, is induced (Schromm et al., 2001, Visintin et al., 2001, Akashi et al., 2001 and Viriyakosol et al., 2001). Schromm et al. clearly demonstrated that MD-2 is an essential molecule for cell response to LPS by making and using MD-2 mutant (Schromm et al., 2001). It is clear based on the function of MD-2 that the polypeptide could be used as an anti-inflammatory agent *in vivo*, a utility specifically stated in the specification as discussed above

and specifically mentioned in at least one of the journal articles (see Viriyakosol et al., page 38060, column 2, last sentence of the Discussion).

Thus, Applicants have included a specific, substantial and credible utility in the specification for the polypeptide of the present invention, namely, use of the polypeptide as an anti-inflammatory agent, and in the treatment and/or prevention of diseases such as septic shock or systemic inflammatory response syndrome (SIRS). Support for this asserted utility is found in the four journal articles filed herewith.

In view of these comments, Applicants assert that the invention has a credible substantial and specific utility, and therefore respectfully request reconsideration and withdrawal of this rejection.

IV. Rejection of Claims Under 35 U.S.C. §112

A. At paragraph 7 of the Office Action, claims 1, 2 and 10 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that as the claimed invention is not supported by a specific or substantial asserted utility or a well-established utility, the skilled artisan would not know how to use the claimed invention.

In response, as discussed above Applicants have demonstrated a specific and substantial asserted utility for the instant invention. Applicants assert that the skilled artisan would readily understand how to make and use the invention as an anti-inflammatory agent for, e.g., the treatment and/or prevention of diseases such as septic shock or systemic inflammatory response syndrome (SIRS).

Accordingly, Applicants assert that the cited claims are fully enabled and thus respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 8 of the Office Action, claims 1 and 10 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that even if the specification were enabling for the polypeptide of SEQ ID NO:7, it would not be enabling for homologues of the protein, including sequences comprising fragments of the protein. The Examiner explains that no biological function, activity or essential properties of the protein of SEQ ID NO:7 are defined in the specification.

In response, Applicants include herewith an amendment to the claims such that a small group of homologues and fragments are recited. Each of the homologues and fragments encompassed within the claims has the same activity as the full length polypeptide of SEQ ID NO:7 (anti-inflammatory activity). In view of the amendment to the claims, Applicants assert that the amended claims are fully enabled and therefore respectfully request the Examiner to reconsider and withdraw the rejection.

C. At paragraph 9 of the Office Action, claims 1 and 10 are rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description in the application as filed.

The Examiner states that the rejected claims are drawn to a genus, i.e., the polypeptide of SEQ ID NO:7 and homologues of this protein. The Examiner contends that the homologues are related to SEQ ID NO:7 only by the method used to identify them, and that there is no indication that they are linked by structure or function to SEQ ID NO:7, and thus there is no indication that they are members of the same genus of proteins.

The Examiner concludes that as the disclosure fails to describe common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID NO:7 is insufficient to describe the genus, and that one skilled in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

In response, Applicants note that, as discussed above, the claims have been amended to recite a small group of homologues and fragments of SEQ ID NO:7 that have the same activity as the polypeptide of SEQ ID NO:7 (anti-inflammatory activity). Thus, the claims recite common attributes or characteristics that identify the members of the genus (i.e., all members of the genus share the same activity and have a similar structure).

In view of the amendment to the claims, Applicants assert that the amended claims have adequate written description support in the application as filed, and therefore respectfully request reconsideration and withdrawal of this rejection.

D. At paragraph 10 of the Office Action, claim 10 is rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that even if the specification were enabling for the polypeptide of SEQ ID NO:7 or a homologue thereof, it would still not reasonably provide enablement for pharmaceutical compositions.

The Examiner explains that as the specification does not provide any guidance as to which, if any, diseases and conditions the protein could be used to treat, it would require undue experimentation for one of skill in the art to use the protein as a therapeutic agent.

In response, as discussed above Applicants have established a utility and activity for the polypeptide of the present application as an anti-inflammatory agent. The specification further discloses diseases that could be treated with the polypeptide of the present invention (i.e., septic shock or systemic inflammatory response syndrome (SIRS)). Applicants assert that the skilled artisan would readily understand how to use the polypeptide of the present invention as an anti-inflammatory agent and in the treatment of disease.

Furthermore, the specification provides support for a pharmaceutical composition for use in treating such diseases or conditions, such as at pages 25-27 of the specification where there is a discussion of the use of the polypeptides of the invention in a medicament.

In view of these comments, Applicants assert that the pharmaceutical compositions recited in claim 10 are fully enabled, and therefore respectfully request reconsideration and withdrawal of this rejection.

E. At paragraph 12 of the Office Action, claims 1 and 10 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that although these claims are drawn to homologues, and a general description of homologues is present on page 5 of the specification, there is no definition that would serve to indicate which proteins would be considered to be homologues and which would not.

In response, Applicants have amended the claims to more clearly recite which homologues are included within the claims (e.g., those with at least 90% homology to SEQ ID NO:7 and having the same activity as the polypeptide of SEQ ID NO:7).

Thus, Applicants assert that the amended claims are definite and therefore respectfully request reconsideration and withdrawal of this rejection.

V. Rejection of Claims Under 35 U.S.C. §102

At paragraph 14 of the Office Action, claims 1, 2 and 10 are rejected under 35 U.S.C. §102(b) as being anticipated by Shimazu et al. (1999).

The Examiner states that Shimazu et al. discloses a protein, MD-2, that is identical to the polypeptide of SEQ ID NO:7. The Examiner states that as the priority is granted to only the filing date of the instant application, the teachings of Shimazu et al. are prior art under 35 U.S.C. §102(b).

As discussed above, Applicants have established a utility for the polypeptide of the present invention. Applicants note that the asserted utility is also set forth in the earliest priority document, namely, Japanese application JP-A-9-274673, filed October 7, 1997, as well as the international application, PCT/JP98/04515, filed October 6, 1998.

In view of the earlier priority date of the Japanese application (October 7, 1997) and the earlier priority date of the international application (October 6, 1998), Applicants respectfully assert that as Shimazu et al. was published (June 7, 1999) well after the priority dates, Shimazu may not serve as legally-effective prior art against the pending claims.

In view of these comments, Applicants respectfully request reconsideration and withdrawal of this rejection.

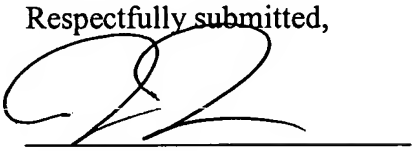
VI. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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